REMARKS

With this reply, claims 26-51 and 59-61 are cancelled, and new claims 62-89 are added. Claims 1-25, 52-58, and 62-89 are pending. Claims 1-3, 5-8, 10-11, 13-14, 17-18, 20, and 22-25 are amended. Support for the amendments can be found throughout the specification, for example, at page 25, FIG. 7, and pages 92-94. No new matter has been added.

Claim Objections

The Examiner has objected to the phrase "to spiking target molecules" in claim 25, suggesting that the phrase is a typographical error. See the Office Action at page 2. Applicants respectfully disagree. The specification, for example at the paragraph bridging pages 37-38, describes addition of target molecules to a sample for purposes of standardization, referred to as "spiking."

Rejection under 35 U.S.C. § 112, second paragraph

Claims 22-23 and 25 have been rejected under 35 U.S.C. § 112, second paragraph for being indefinite. See the Office Action at page 2. In particular, the Examiner argues that the phrases "target molecules arranged on at least one array element" in claim 22 and "in sufficient concentration" in claim 25 are unclear. Claim 23 depends from claim 22.

Claim 22 has been amended to make clear that the phrase "arranged on at least one array element" describes the fourth probe molecules, not target molecules.

Claim 25 has been amended to make clear that the fifth probe molecules have a specific affinity to spiking target molecule added externally to the sample, or to a target molecule present in the sample in sufficient concentration to lead to a clearly detectable signal. See the specification, for example, at page 38.

Applicants believe the amendments to claims 22 and 25 overcome the rejection under § 112, second paragraph, and respectfully ask the Examiner to reconsider and withdraw the rejection.

Rejection under 35 U.S.C. § 102(b)

Claims 1-15 have been rejected as being anticipated by U.S. Patent No. 5,700,642 to Monforte et al. ("Monforte"). See the Office Action at page 3-4. Claim 1 is independent and claims 2-15 depend from it.

Applicants have discovered a probe array for qualitative and/or quantitative detection of target molecules in a sample by molecular interactions between probe molecules and target molecules on the probe array. The probe array includes an array surface, a first cleavage product of a first probe molecule which includes a label, and a second cleavage product of the first probe molecule which is immobilized on the array surface. **The first cleavage product is bound to a first region of a target molecule, and the second cleavage product is bound to a second region of the target molecule**. The array also includes a cleavage product of a second probe molecule immobilized on the array surface at a second defined site, wherein the cleavage product of the second probe molecule is not bound to a target molecule. See independent claim 1. By way of illustration, see also FIG. 7.

Monforte describes modified oligonucleotide primers. The primers can be extended from its 3' portion, immobilized at a 5' portion, and cleaved so that **the extended 3' end is released from the immobilized 5' portion**. See Monforte, for example, at Abstract, and at column 5, lines 46-48 ("The first primer is then cleaved from the immobilized product at the cleavable site, causing release of the extension segment from the support."). However, Monforte does not teach that **a first cleavage product is bound to a first region of a target molecule, and the second cleavage product is bound to a second region of the target molecule**. Instead, Monforte teaches that after cleavage, the 3' end remains associated with the 5' portion that it had been linked to (See Monforte at FIG. 6A-6B, showing steps of denaturing and washing before cleavage, so that a single stranded, immobilized primer undergoes cleavage).

Thus Monforte does not teach all the limitations of claim 1, nor the claims that depend from it. Accordingly, Applicants respectfully ask that the Examiner reconsider and withdraw the rejection under § 102(b).

Rejections under 35 U.S.C. § 103(a)

Fung

Claims 1 and 15-16 have been rejected as being obvious over Monforte in view of U.S. Patent No. 4,757,141 to Fung et al. ("Fung"). See the Office Action at page 5-6. Claims 15 and 16 depend from claim 1.

As discussed above, Monforte fails to teach all the limitations of independent claim 1. In particular, Monforte does not teach a probe array in which **a first cleavage product is bound to a first region of a target molecule, and the second cleavage product is bound to a second region of the target molecule**. Fung does not remedy this defect.

Fung is directed generally to amino-derivatized phosphite and phosphate linking agents (see Fung at Title). Nothing in Fung teaches, suggests, or motivates a person having ordinary skill in the art to make probe array in which **a first cleavage product is bound to a first region of a target molecule, and the second cleavage product is bound to a second region of the target molecule**.

Applicants also respectfully disagree Fung teaches a detectable unit is coupled to probe molecules via an anchor group. The specification at page 40 describes that "the anchor groups are reacted with **specifically binding** components . . . which are detectable themselves or trigger a detectable reaction." The linking agents described in Fung do not engage in any specific binding. Rather, Fung teaches reagents that undergo covalent bond-forming reactions.

Because Monforte in view of Fung does not teach all of the limitations of claims 1, 15, and 16, Applicants respectfully seek reconsideration and withdrawal of the rejection.

Lockhart

Claims 1, 17-18 and 22-25 have been rejected as being obvious over Monforte in view of U.S. Patent No. 6,040,138 to Lockhart et al. ("Lockhart"). See the Office Action at pages 6-9. Claims 17-18 and 22-25 depend from claim 1.

As discussed above, Monforte fails to teach all the limitations of independent claim 1. In particular, Monforte does not teach a probe array in which **a first cleavage product is bound to**

a first region of a target molecule, and the second cleavage product is bound to a second region of the target molecule. Lockhart does not remedy this defect.

Lockhart does not describe probe molecules including cleavable bonds; accordingly, Lockhart does not describe cleavage products of probe molecules. Additionally, throughout Lockhart, it is the non-immobilized member of a hybridized pair (i.e., the target) of nucleic acids that carries the label. See Lockhart, for example, at column 13, line 36 to column 14, line 36 (section titled "Labeling Nucleic Acids"). Nowhere does Lockhart describe a probe array capable of having **a first cleavage product is bound to a first region of a target molecule, and the second cleavage product is bound to a second region of the target molecule**.

With regard to claim 17, the Examiner asserts that Lockhart's mismatch control probes are "second probe molecules that are labeled and have no selectively cleavable bond." See the Office Action at 7. Applicants respectfully disagree. As discussed, Lockhart does not describe any immobilized, labeled probes.

With regard to claim 22, the Examiner argues that Lockhart's expression level control probes "hav[e] no specific affinity to target molecules." See the Office Action at page 8. Applicants respectfully disagree. Lockhart at column16, lines 33-35, quite unambiguously teaches that "[e]xpression level controls are probes that hybridize specifically with constitutively expressed genes."

For at least the reasons given, Monforte in view of Lockhart does not teach all the limitations of claims 1, 17-18 and 22-25. Applicants respectfully ask that the rejection be reconsidered and withdrawn.

Mackay

Claims 1 and 19 have been rejected as being obvious over Monforte in view of U.S. Patent No. 5,700,642 to Mackay ("Mackay"). See the Office Action at pages 9-10. Claim 19 depends from claim 1.

As discussed above, Monforte fails to teach all the limitations of independent claim 1. In particular, Monforte does not teach a probe array in which **a first cleavage product is bound to**

a first region of a target molecule, and the second cleavage product is bound to a second region of the target molecule. Mackay does not remedy this defect.

Mackay is directed to visualization of spots in an electrophoretic gel using a charge-coupled device (see Mackay at Abstract). Nothing in Mackay teaches, suggests, or motivates a person having ordinary skill in the art to make probe array in which **a first cleavage product is bound to a first region of a target molecule, and the second cleavage product is bound to a second region of the target molecule**.

In addition, Mackay does not teach a cleavage product of a probe molecule immobilized on an array surface at a defined site. Instead, Mackay relates to visualization of spots in an electrophoretic gel, a technique which requires that the molecules to be detected are mobile and not immobilized.

For at least the reasons given, Monforte in view of Mackay does not teach all the limitations of claims 1 and 19. Applicants respectfully ask that the rejection be reconsidered and withdrawn.

Lockhart and Kievits

Claim 20 has been rejected as being obvious over Monforte and Lockhart in view of U.S. Patent No. 5,770,360 to Kievits et al. ("Kievits"). See the Office Action at pages 10-11.

As discussed above, Monforte (alone, or in combination with Lockhart) fails to teach all the limitations of independent claim 1. In particular, Monforte does not teach a probe array in which **a first cleavage product is bound to a first region of a target molecule, and the second cleavage product is bound to a second region of the target molecule**. Kievits does not remedy this defect.

Kievits is directed to elimination of false negatives in detection of amplified nucleic acids. Nothing in Kievtis teaches, suggests, or motivates a person having ordinary skill in the art to make probe array in which **a first cleavage product is bound to a first region of a target molecule, and the second cleavage product is bound to a second region of the target molecule**.

Nor does Kievits teach the limitation for which it is cited. The Examiner argues that Kievits teaches probe molecules "which differ in their labeling degree (e.g., the probes are labeled differently [column 5, lines 32-37]; therefore the first probe is labeled to a high degree with a first label but not a second label, and vice versa for the second probe)." See the Office Action at page 11. Applicants respectfully disagree. The specification explains how probes differ in their degree of labeling "for example with a defined mixture of labeled and unlabelled probes varying in the form of a dilution series from array element to array element." In order to normalize a measurement, "the values of the detection standard elements . . . are plotted against the mixing ratio of labeled and unlabelled substance. This results in a calibration curve which indicates the dynamic range and the type of interdependence between the quantity of detectable units." (specification at 58-59).

The relevant portion of Kievits reads:

> In order to detect whether the analyte or the internal control is bound to the solid phase, two differently labeled detection probes now can be used. One will react specifically with the analyte bound to the solid phase . . . while **the second labeled detection probe, comprising a label that can be distinguished from the label on the first detection probe**, will react specifically with the internal control. The internal control used in this case must resemble the analyte in its capability of hybridizing to the immobilized oligonucleotide on the solid phase, but must differ from the analyte in that it will react with a different labeled detection probe than the analyte.

Kievits at column 5, lines 24-37 (emphasis added). Kievits teaches a difference in kind—the labels can be distinguished from one another—not a difference in degree.

For at least the reasons given, Monforte and Lockhart in view of Kievits do not teach all the limitations of claim 20. Applicants respectfully ask that the rejection be reconsidered and withdrawn.

Mackay and Kievits

Claim 21 has been rejected as being obvious over Monforte and Mackay in view of Kievits. See the Office Action at pages 11-12.

As discussed above, Monforte (alone, or in combination with Mackay) fails to teach all the limitations of independent claim 1. In particular, Monforte does not teach a probe array in which **a first cleavage product is bound to a first region of a target molecule, and the second cleavage product is bound to a second region of the target molecule**. Kievits does not remedy this defect.

Kievits is directed to elimination of false negatives in detection of amplified nucleic acids. Nothing in Kievits teaches, suggests, or motivates a person having ordinary skill in the art to make probe array in which **a first cleavage product is bound to a first region of a target molecule, and the second cleavage product is bound to a second region of the target molecule**.

Furthermore, as discussed above, Kievits does not teach detectable units arranged on different array elements which differ in their labelling degree.

For at least the reasons given, Monforte and Mackay in view of Kievits do not teach all the limitations of claim 21. Applicants respectfully ask that the rejection be reconsidered and withdrawn.

Stratagene Catalog

Claims 52-58 have been rejected as being obvious over Monforte in view of the 1998 Stratagene Catalog ("the catalog"). See the Office Action at pages 12-14. Claims 52-58 depend from claim 1.

As discussed above, Monforte fails to teach all the limitations of independent claim 1. In particular, Monforte does not teach a probe array in which **a first cleavage product is bound to a first region of a target molecule, and the second cleavage product is bound to a second region of the target molecule**. The catalog does not remedy this defect.

The catalog describes various gene characterization kits, but nothing in the catalog teaches, suggests, or motivates a person having ordinary skill in the art to make probe array in which **a first cleavage product is bound to a first region of a target molecule, and the second cleavage product is bound to a second region of the target molecule**.

For at least this reason, Applicants believe claims 52-58 are patentable over Monforte in view of the catalog. Reconsideration and withdrawal of the rejection is respectfully sought.

New claims

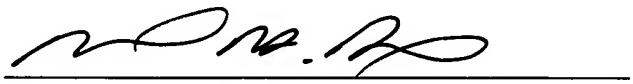
New claims 62-89 have been added. Claims 62 and 87 are independent. Claims 63-86 depend from claim 62, and claims 88-89 from claim 87. Support for the new claims can be found, for example, at page 25, FIG. 7, and pages 92-94. Applicants assert that none of the art of record teaches the limitations of the new claims. Applicants respectfully ask that the new claims be allowed.

CONCLUSION

Applicants ask that all claims be allowed. If the Examiner believes it to be helpful, the Examiner is invited to contact the undersigned representative by telephone at 202-429-3000. Please apply any charges or credits to deposit account 19-4293.

Respectfully submitted,

Date: 2-21-07



Harold H. Fox
Reg. No. 41,498

Steptoe & Johnson LLP
1330 Connecticut Avenue, NW
Washington, DC 20036-1795
Phone: 202-429-3000
Fax: 202-429-3902